

# Dynamic changes in liver stiffness measurements using transient elastography in hemodialysis patients

 Nottawan Suksai<sup>1</sup>,  Somchai Yongsiri<sup>2</sup>,  Raweevan Witoon<sup>2</sup>,  Rachaneeporn Chueansuwan<sup>1</sup>,  Anothai Juttuporn<sup>3</sup>

<sup>1</sup>Division of Gastroenterology, Department of Medicine, Burapha University, Chonburi, Thailand; <sup>2</sup>Division of Nephrology, Department of Medicine, Burapha University, Chonburi, Thailand; <sup>3</sup>Department of Preventive Medicine and Family Medicine, Burapha University, Chonburi, Thailand

## Abstract

**Background and Aim:** The impact of fluid status changes on liver stiffness measurements (LSM) using transient elastography (TE) in dialysis patients remains unclear. This study aimed to evaluate LSM variations during hemodialysis (HD) and analyze contributing factors.

**Materials and Methods:** A cross-sectional study was conducted on dialysis patients at a tertiary care hospital. TE and bioelectrical impedance analysis were performed at four time points: before dialysis, immediately after, the first day after, and the second day after dialysis. LSM values were compared across these time points.

**Results:** Seventy patients were enrolled, with two cases showing consistently extremely elevated LSM values exceeding 20 kPa, considered outliers. The mean LSM values were 7.6±7.0 kPa before dialysis, 6.12±2.94 kPa immediately after, 6.64±5.27 kPa on the first day, and 6.94±5.12 kPa on the second day after dialysis. The mean pre-HD LSM was significantly higher than immediately after and on the first day after dialysis, with mean differences of 1.54 kPa (95% CI 0.22–2.86, p=0.02) and 1.02 kPa (95% CI 0.15–1.9, p=0.02), respectively. The ultrafiltration volume positively correlated with the LSM difference pre- and post-HD (r=0.315, p=0.008). Patients with residual fluid overload had significantly higher post-HD LSM compared to euvolemic patients (p=0.003).

**Conclusion:** LSM values significantly decreased after dialysis and remained lower for up to 24 hours. Transient elastography should preferably be performed within 24 hours post-dialysis when the patient is in a euvolemic state.

**Keywords:** Hemodialysis; liver fibrosis; transient elastography.

## Introduction

The prevalence of significant hepatic fibrosis in chronic kidney disease (CKD) exceeds 20%, often linked to hepatitis B, hepatitis C, and metabolic dysfunction-associated steatotic liver disease (MASLD).<sup>[1–9]</sup> The gold stan-

dard for evaluating hepatic fibrosis is liver biopsy, but it carries risks such as intra-abdominal bleeding.<sup>[10,11]</sup> Transient elastography (TE), a widely validated non-invasive tool, has demonstrated superior reliability over other non-invasive methods for predicting liver fibrosis in CKD patients.<sup>[12–16]</sup>

TE provides essential insights into liver integrity, often reflecting fibrosis. However, erroneously high LSM can occur in cases of acute hepatitis, cholestasis, ascites, excessive alcohol intake, and elevated central venous pressure, the latter of which is potentially associated with hepatic congestion.<sup>[17–23]</sup> In dialysis patients, fluid shifts may affect LSM results, leading us to hypothesize that LSM values vary throughout the dialysis session. Studies on LSM in dialysis patients have shown inconsistent results, and most included small population groups.<sup>[24–27]</sup> No data exists on LSM changes between dialysis sessions. This study aimed to assess whether LSM values differ before, immediately after, and between dialysis sessions.

## Materials and Methods

This was a cross-sectional study conducted between January 15, 2024, and April 30, 2024, at the hemodialysis center of a tertiary-care hospital. The Burapha University Ethics Committee authorized the study protocol in accordance with the Helsinki Declaration (approval No: IRB1-117/2566). Prior to data collection, each participant provided written informed consent.

## Patients

Inclusion criteria were Thai patients with end-stage renal disease (ESRD) aged 18 years or older undergoing regular hemodialysis (HD). Exclusion criteria included body mass index >30 kg/m<sup>2</sup>, elevated aspartate and alanine aminotransferase levels >3times the upper limit of normal, total bilirubin >3.5 mg/dL, ascites, sepsis, heart failure, hepatobiliary cancer, and inability to undergo a reliable TE examination, as these factors could lead to errors in TE measurements.

Medical history and ultrafiltration volume were documented, along with measurements of height, weight, and waist circumference. Laboratory tests included liver chemistry, complete blood count, creatinine, coagulogram, iron profile, lipid profile, blood glucose, and serologic markers for hepatitis B and C.

## Procedure

Participants underwent liver stiffness measurement using TE and body fluid assessment via bioelectrical impedance analysis (BIA) at four time points: within 1 hour before dialysis, immediately after (within 6 hours), 24 hours after, and 48 hours after dialysis.

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**Corresponding author:** Nottawan Suksai; Division of Gastroenterology, Department of Medicine, Burapha University, Chonburi, Thailand  
**Phone:** +6687 330 4172; **e-mail:** nottawan@go.buu.ac.th

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**Table 1.** Baseline characteristics of the study population (n=70)

Demographic characteristics	
Age (years)	57.4±15.4
Sex (male), n (%)	35 (50)
Weight	
Pre-HD (kg)	65.15±14.53
Post-HD (kg)	62.36±14.08
Body mass index (kg/m <sup>2</sup> )	23.5±4.27
Waist circumference (cm)	90.5±17.9
Comorbidity*, n (%)	
Metabolic syndrome	64 (91.4)
Cardiovascular disease	21 (30)
Chronic liver disease*, n (%)	
MASLD	3 (4.3)
Hepatitis B	0 (0)
Hepatitis C	0 (0)
Cirrhosis	
CTP A	1 (1.4)
CTP B	2 (2.9)
History of high-volume alcohol consumption, n (%)	7 (10)
Etiology of ESRD*, n (%)	
Diabetic nephropathy	31 (44.3)
Hypertensive nephropathy	21 (30)
Other causes	18 (25.7)
Hemodialysis	
Ultrafiltration volume per HD session (liters)	3.13±1.2
Percent of interdialytic weight gain (%)	4.58±2.2

Data are displayed as the mean (±SD) and number (%). \*: This data was obtained from medical records and documented diagnoses. MASLD: Metabolic dysfunction-associated steatotic liver disease; CTP: Child-turcotte-pugh; ESRD: End-stage renal disease; HD: Hemodialysis.

Liver stiffness was measured with a Fibroscan (Echosens®, Paris, France) by a single certified operator, using the same device throughout. Calibration followed manufacturer guidelines. Reliability required ten valid LSMs, a success rate ≥60%, and an interquartile range/median ratio <0%.<sup>[28]</sup> TE provides two parameters: liver stiffness measurement (LSM, kPa) reflecting liver elasticity, and controlled attenuation parameter (CAP, dB/m), indicating liver fat content. Significant fibrosis was defined as LSM ≥8 kPa, advanced fibrosis as LSM ≥12 kPa, and fatty liver as CAP ≥275 dB/m.<sup>[14,15]</sup>

BIA was used to assess body fluid status, utilizing a multifrequency bioimpedance spectroscopy device (BCM®; Fresenius Medical Care, Bad Homburg, Germany). Body fluid composition and overhydration (OH) values were recorded, with patients classified as fluid overloaded if OH was ≥1.1.<sup>[29]</sup>

### Outcomes

The primary outcome was the difference in LSM at four time points, including before dialysis, immediately after, the first day, and the second day after dialysis.

Secondary outcomes included correlations between ultrafiltration volume and percentage of interdialytic weight gain with the difference in LSM before and immediately after dialysis; the relationship of body

**Table 2.** Laboratory results of the study population (n=70)

Laboratory results	
Aspartate aminotransferase (U/L)*	18.5 (14, 25)
Alanine aminotransferase (U/L)*	14 (9, 22)
Alkaline phosphatase (U/L)*	92 (78, 120)
Total bilirubin (mg/dL)*	0.4 (0.3, 0.7)
Direct bilirubin (mg/dL)*	0.2 (0.2, 0.3)
Albumin (g/dL) <sup>†</sup>	3.87±0.49
Creatinine (mg/dL) <sup>†</sup>	8.96±3.69
Blood urea nitrogen (mg/dL) <sup>†</sup>	68.57±24.79
Hematocrit (%) <sup>†</sup>	31.76±4.74
White blood cell count (x10 <sup>9</sup> /μL) <sup>†</sup>	7214.4±2123.96
Platelet count (x10 <sup>9</sup> /μL) <sup>†</sup>	2.2±0.7
International normalized ratio (INR) <sup>†</sup>	1.15±0.29
HBsAg, n (%) <sup>‡</sup>	0 (0%)
Positive total anti-HBc antibody, n (%) <sup>‡</sup>	8 (11.4%)
Positive anti-HCV antibody, n (%) <sup>‡</sup>	0 (0%)
Ferritin (ng/mL)*	421 (246, 882)
Percent of transferrin saturation (%) <sup>*</sup>	2.9 (2.0, 3.6)
Hemoglobin A1C (%) <sup>†</sup>	6.33±1.59
Triglyceride (mg/dL)*	113 (84, 164)
High-density lipoprotein (mg/dL) <sup>†</sup>	49.96±15.26
Low-density lipoprotein (mg/dL) <sup>†</sup>	103.04±45.08

Data are displayed as the mean (±SD)<sup>†</sup>, median (interquartile range)<sup>\*</sup>, and number (%)<sup>‡</sup>.

fluid volume with post-HD LSM; changes in CAP across the four time points; and the prevalence of significant fibrosis and fatty liver in dialysis patients.

### Statistical Analysis

The sample size was determined to be at least 45 patients using a paired means formula,<sup>[30]</sup> with a pre- and post-HD LSM difference of 7.3 kPa and a standard deviation of 17.31 based on a prior study.<sup>[27]</sup> Patient characteristics were summarized with mean or median for continuous variables and frequency and percentage for categorical variables. Differences in LSM and CAP across the four time points were analyzed using Repeated Measures ANOVA or Friedman’s test.

Spearman’s correlation coefficient (r) assessed the relationship between the mean ultrafiltration volume, percentage of interdialytic weight gain, and LSM differences pre- and post-dialysis. The Mann-Whitney U test or paired t-test compared LSM between patients with fluid overload and those in a euvolemic state post-dialysis. The prevalence of significant liver fibrosis and fatty liver disease was reported as percentages. A p-value <0.05 was considered statistically significant.

## Results

### Patient Characteristics

Seventy patients were enrolled, with characteristics summarized in Table 1. The mean age was 57.4±15.4 years. Metabolic syndrome and cardiovascular disease were the most common comorbidities. Three patients had cirrhosis due to metabolic dysfunction-associated steatotic

**Table 3.** The difference of liver stiffness measurement values during dialysis sessions

Timing related to HD	LSM values	Mean difference (kPa)	Standard error	95% CI		p
				Lower bound	Upper bound	
Before HD	Immediately after	1.54*	0.66	0.22	2.86	0.02
	First day	1.02*	0.43	0.15	1.88	0.02
	Second day	0.72	0.44	-0.16	1.59	0.11
Immediately after	Before HD	-1.54*	0.66	-2.9	-0.22	0.02
	First day	-0.52	0.53	-1.58	0.53	0.32
	Second day	-0.83	0.51	-1.84	0.19	0.11
First day	Before HD	-1.02*	0.43	-1.88	-0.15	0.02
	Immediately after	0.52	0.53	-0.53	1.58	0.32
	Second day	-0.30	0.22	-0.74	0.14	0.18
Second day	Before HD	-0.72	0.44	-1.59	0.16	0.11
	Immediately after	0.83	0.51	-0.19	1.84	0.11
	First day	0.30	0.22	-0.14	0.74	0.18

Data are presented as mean values. \*: Indicates statistical significance. LSM: Liver stiffness measurement; CI: Confidence interval; HD: Hemodialysis; kPa: Kilopascal.

**Table 4.** Body fluid composition

Parameters	Pre-HD (L)	Intermediately after HD (L)	First day after HD (L)	Second day after HD (L)
Total body water <sup>†</sup>	32.81±7.17	30.83±6.85	31.38±6.82	32.47±6.94
Extracellular water <sup>†</sup>	15.97±3.59	13.94±3.05	14.74±3.19	15.59±3.25
Intracellular water <sup>†</sup>	16.77±3.99	16.86±4.21	16.61±3.87	16.73±4
Over dehydration (OH)*	1.8 (1.1, 3)	-0.2 (-0.9, 1.1)	0.8 (0, 1.9)	1.4 (0.6, 2.8)

Data are displayed as the mean (±SD)<sup>†</sup> or median (interquartile range)\*. HD: Hemodialysis; L: Liter.

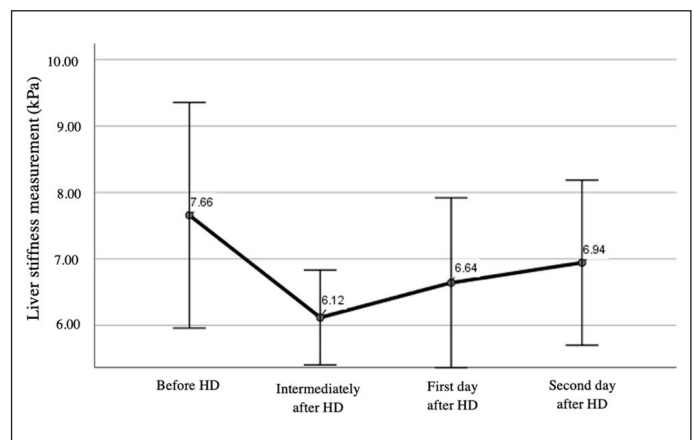
liver disease, with one case confirmed by liver biopsy. No patients had hepatitis B or C; however, eight tested positive for total anti-HBc. Laboratory results are detailed in Table 2.

### Liver Stiffness Measurement

Two patients had extremely high LSM values (>20 kPa) across all four time points and were considered outliers. The mean LSM values for the remaining patients were 7.6±7.0 kPa before dialysis, and 6.12±2.94 kPa, 6.64±5.27 kPa, and 6.94±5.12 kPa immediately after, the first day after, and the second day after dialysis, respectively, as shown in Figure 1.

The pre-dialysis LSM remained significantly higher than the immediately post-HD and one-day post-HD values, with mean differences of 1.54 kPa (95% CI 0.22–2.86, p=0.02) and 1.02 kPa (95% CI 0.15–1.9, p=0.02), respectively, as detailed in Table 3. Dynamic changes of LSM for all patients are shown in Figure 2.

The mean ultrafiltration volume was 3.13±1.2 liters, which was correlated with the difference between pre-HD and immediately post-HD LSM values (r=0.315, p=0.008). The percentage of interdialytic weight gain did not correlate significantly with the LSM difference between pre- and post-HD (r=0.232, p=0.053). Patients with residual fluid overload post-hemodialysis (OH ≥1.1) had significantly higher post-HD LSM compared to the euvoletic group (OH <1.1), with values of 7.1 (5.1, 11.3) kPa versus 4.9 (4.2, 6.2) kPa, p=0.003. Body fluid composition data are presented in Table 4.

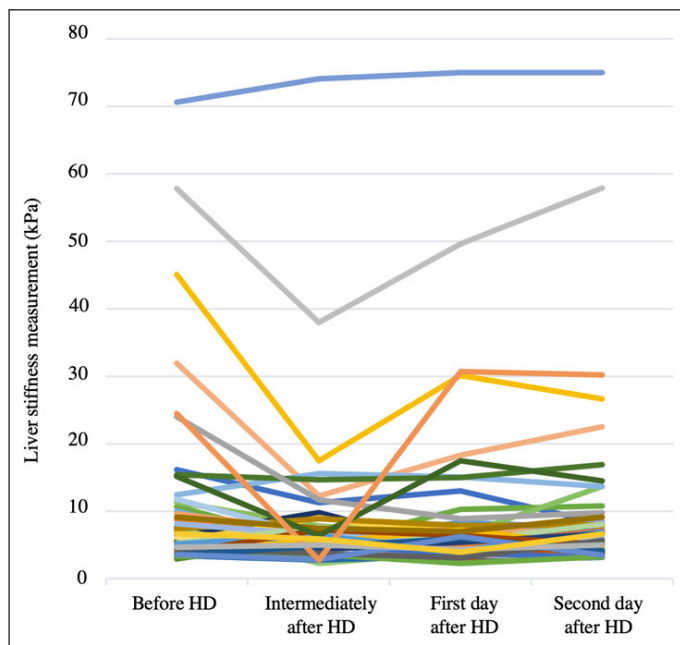


**Figure 1.** The mean liver stiffness measurement values at the different time points during the dialysis session.

Data are displayed as the mean (±standard error). HD: Hemodialysis; kPa: Kilopascal.

### Controlled Attenuation Parameter (CAP)

The mean CAP values were 190.53 dB/m before dialysis, 210.97 dB/m immediately after, 198.59 dB/m on the first day, and 195.80 dB/m on the second day after dialysis. The CAP value immediately after dialysis was significantly higher than at the other time points (p<0.05).



**Figure 2.** Changes in liver stiffness measurement values at the different time points during the dialysis session.

Data for all seventy patients are presented as mean values. HD: Hemodialysis; kPa: Kilopascal.

### Prevalence of Significant Fibrosis and Fatty Liver

In this end-stage renal disease population, the prevalence of significant liver fibrosis was 15.7%, with advanced fibrosis present in 54.5% of these cases. MASLD was identified in 14.3% of patients based on baseline metabolic syndrome criteria and CAP  $\geq 275$  dB/m.

### Discussion

Our study demonstrated dynamic changes in LSM among hemodialysis patients. LSM values significantly decreased after dialysis, with reductions lasting up to 24 hours. Patients with persistent fluid overload had higher post-dialysis LSM, and the mean ultrafiltration volume correlated with pre- and post-HD LSM differences. We also tested for the ultrafiltration volume (UF) cut point affecting LSM differences and found that a UF of just 0.5 L led to lower LSM after dialysis. CAP value changes were observed, though these differences likely have no clinical impact but may inform future research.

Although our data may not follow a normal distribution, a parametric test was used due to the observed trend in LSM changes across repeated measurements, which could become more pronounced in a larger population. Two patients with consistently high LSM ( $>20$  kPa) at all time points were considered outliers to improve data precision, as their changes were unlikely to impact treatment decisions.

Our study results support that the increase in LSM was related to fluid overload, which is hypothesized to be caused by hepatic congestion. Khunpakdee et al.<sup>[26]</sup> studied 36 patients and found no overall difference in pre- and post-HD LSM but noted post-HD LSM decreases in patients with a UF  $>2.5$  L. Taneja et al.<sup>[27]</sup> demonstrated decreased LSM values post-HD in a larger population. Liver biopsies were performed on 18 of the 68 patients, suggesting that post-HD LSM may more accurately predict liver fibrosis. Liu et al.<sup>[16]</sup> compared post-dialysis LSM

with liver biopsy in 284 patients, reporting a post-HD LSM cutoff of 7.1 kPa with 55% sensitivity and 96% specificity for predicting significant fibrosis, and 8.3 kPa with 95% sensitivity and 99% specificity for advanced fibrosis. Our study extends this research by assessing LSM at multiple dialysis time points.

Considering our study results alongside prior data, post-dialysis LSM assessment appears to be the optimal time point for LSM evaluation. TE can be performed after dialysis, when patients reach euvolemic status, up to one day post-dialysis, allowing convenient scheduling. In our population, post-HD LSM generally decreased slightly in most patients, likely with minimal clinical impact. However, patients with very high pre-HD LSM showed substantial decreases post-HD. High LSM influences clinical decisions, such as initiating antiviral therapy, conducting hepatocellular carcinoma surveillance, and considering transplantation. LSM measurements during fluid overload may overestimate liver fibrosis, potentially affecting patient care. Awareness of reduced LSM post-dialysis may help prevent misinterpretation of liver health. Falsely low LSM should also be considered in cases of excessive fluid removal causing hypovolemia during HD.

A limitation of our study is the lack of histologic confirmation. However, strengths include assessment at multiple time points, a sufficient sample size, and comprehensive fluid status evaluation. Future studies on dialysis patients with chronic liver disease could further clarify the impact of fluid shifts on LSM accuracy in this population.

### Conclusion

LSM values decreased post-dialysis and remained lower for up to 24 hours. TE interpretation should always consider patients' fluid status to ensure accurate assessment.

**Ethics Committee Approval:** The Burapha University Ethics Committee granted approval for this study (date: 28.11.2023, number: IRB1-117/2566).

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